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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,425	09/16/2003	Paola Minoprio	03495-0200-01000	8191
22852	7590	09/20/2005	EXAMINER	
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413			FORD, VANESSA L	
		ART UNIT	PAPER NUMBER	
		1645		

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/662,425	MINOPRIO ET AL.
	Examiner Vanessa L. Ford	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 16 September 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 79-82 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 79-82 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 16 September 2003 is/are: a) accepted or b) objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date: _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>1/7/2004</u> .	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

Specification

1. The substitute specification filed September 16, 2003 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: The substitute specification must be submitted with markings showing all the changes relative to the immediate prior version of the specification of record. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. An accompanying clean version (without markings) and a statement that the substitute specification contains no new matter must also be supplied. Numbering the paragraphs of the specification of record is not considered a change that must be shown. A substitute specification must not contain new matter.

Claim Objection

2. Claims 79-82 are objected to for the following informalities: The claims should be the subject of a complete sentence and the claims should also state "What is claimed is ..." or "We claim ..." Correction is required.

Drawings

3. The Drawings are objected to for the following reasons: The figures should correspond to the text as set forth in the Brief Description of the Drawings. For example, Figure 5 should recite "Figure 5A", and "Figure 5B" in the Brief Description of the Drawings and so forth. It should be also noted that sequences on pages 86-96 have not been identified in the instant specification. Correction and/or clarification is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 79-82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,713, 617 B1 published March 30, 2004. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5 of issued patent no. 6,713, 617 B1 would be a species of nucleic acid molecules that are encompassed by the genus of nucleic acid molecules claimed in the instant application.

Since the nucleic acid molecules claimed in the instant application encompass variants, homologs, degenerates, derivatives, fragments of SEQ ID NO: 7 as well as the nucleic acid molecule as set in the nucleic acid sequence of SEQ ID NO:7.

The Examiner is interpreting the claimed invention as a purified nucleic molecule that hybridizes to a DNA molecule comprising the nucleic acid sequence of SEQ ID NO:7 under moderate stringency conditions and encodes an amino acid racemase activity or a molecule that is derived from SEQ No:7 and encodes an amino acid racemase activity or a molecule that is a degenerate of SEQ ID NO:7 and encodes an amino acid racemase activity. Therefore, the claimed molecule broadly encompasses fragments as well as variants of SEQ ID NO:7.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 79-82 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:7, does not reasonably provide enablement for variants, homologs, degenerates derivatives or fragments of SEQ ID NO:7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 79-82 are directed to a purified nucleic acid molecule comprising:

(a) a molecule that hybridizes to either strand of a denatured, double-stranded DNA comprising the nucleic acid molecule of SEQ ID NO:7 under conditions of moderate stringency and that encodes an amino acid racemase activity; and/or (c) a molecule that is degenerate from SEQ ID NO:7 as result of the genetic code and that encodes an amino acid racemase activity and a recombinant vector, host cell and kit comprising the nucleic acid molecule.

The specification contemplates nucleic acid molecules that are variants or fragments of SEQ ID NO:7 (page 5). The specification teaches that fragments of SEQ ID NO: 7 can contain form 15 to 40 nucleotides (page 5).

There is no guidance provided as to which nucleic acids can be added, deleted or substituted and the polynucleotide retain its biological function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the nucleic acid sequence of the polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar activity requires a knowledge with regard to which nucleic acids in the polynucleotide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polynucleotide's structure relates to function. However, the problem of the prediction of polynucleotide's structure from mere sequence data of a single polynucleotide and in turn utilizing predicted

structural determinations to ascertain functional aspects of the polynucleotide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substitutions or multiple modifications of other types and the positions within the polynucleotide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polynucleotide and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modifications, e.g., multiple substitutions. The sequence of some polynucleotide is highly conserved and one skilled in the art would not expect tolerance to any nucleic acid modification in such polynucleotides.

The following references provide evidence that the modifications in the nucleic acid sequence directly effects the gene product expressed.

Kleppe et al (*Tidsskr Nor Laegeforen*, September 30, 2001; 121(23):2717-20) teach that the main function of DNA is to code for protein, it is logical to examine the impact of mutations on protein structure and function (see the Abstract).

Hoppner (*Horm Re. 2002, 58 Suppl. 3:7-15*) teaches that genetic aberrations, like chromosomes aneuploidy, gene translocations or mutations in key regulatory proteins often lead to clinical symptoms (see the Abstract). Hoppner teaches that minor genetic alterations like point mutations can affect the function of gene products (see the Abstract). Therefore base upon the teaching of the cited art, one of skill in the art could conclude that modifying a nucleic acid molecule has a direct effect on the protein and

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the function of the protein that is encoded by the nucleic acid molecule. In the instant case, modifications along the DNA molecule could result in a protein encoded by the nucleic acid molecule that does not have the desired biological function (i.e. racemase activity).

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting other nucleic acid molecules having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use polynucleotides that are variants, homologs, degenerates, derivatives or fragments of SEQ ID NO: 7 in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation to is undue.

The Applicant has not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions

and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the nucleic acid's structure and still maintain activity is unpredictable and the experimentation left those skilled in the art is unnecessarily and improperly, extensive and undue. See Amgen Inc v Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S. P.Q. 546(Bd. Pat=, App & int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention commensurate in scope with the claims.

6. Claims 79-82 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule that encode proteins that have proline racemase activity does not reasonably provide enablement for nucleic acid molecules that encode proteins that any racemase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 79-82 are directed to a purified nucleic acid molecule comprising:

(a) a molecule that hybridizes to either strand of a denatured, double-stranded DNA comprising the nucleic acid molecule of SEQ ID NO:7 under conditions of moderate stringency and that encodes an amino acid racemase activity; and/or (c) a molecule that is degenerate from SEQ ID NO:7 as result of the genetic code and that encodes an

amino acid racemase activity and a recombinant vector, host cell and kit comprising the nucleic acid molecule.

The claimed invention broadly encompasses nucleic acid molecules that encode proteins that have any racemase activity. The specification teaches that SEQ ID No.7 represents the full nucleotide sequence and its corresponding polypeptide sequence coding for a proline racemase of *Trypanosoma cruzi* (page 5). Examples 14 and 15 of the instant specification shows racemization assays (pages 65-66). These examples show that the protein encoded by the nucleic acid sequence of the claimed invention has proline racemase activity. The instant specification is not enabled for any other racemase activity.

The following art references are cited regarding eukaryotic racemase activity:

Chamond et al (*The Journal of Biological Chemistry*, Vol. 278, Issue of May 2, pp. 15484-15494, 2003) teach that there are a variety of racemases have been demonstrated in bacteria and fungi (page 15484). Chamond et al teach that eukaryotic proline racemase has been isolated from the infective metacyclic forms of *Trypanosoma cruzi* (page 15484). Cook et al (*The Journal of Biological Chemistry*, Vol. 277, No. 31, August 2, 2002, pages 27782-27792) teach that serine racemase is a brain enzyme present in glial cells (see the Abstract). Cook et al suggests that eukaryotic serine racemase activity is modulated by calcium levels *in vitro* (see the Abstract and page 27791). Cook et al discloses that alanine racemases exist and are inhibited by alanine phosphonic acid (page 27790). Cheng et al (*The Journal of Biological Chemistry*, Vol. 276, No., February 18, 2000, pages 4906-4911) teach that a eukaryotic alanine racemase is involved in cyclic peptide biosynthesis (see the Title and the Abstract).

The cited art references have taught that other eukaryotic racemases such as serine racemase and alanine racemase exists. Therefore, one of skill in the art would reasonably conclude that the claimed nucleic acid molecules do not encode proteins that have "any" or "all" racemase activity. One of skill in the art would conclude from the teachings of the specification and the cited art that the instant specification is only enabled for purified nucleic molecules that encode proteins that have proline racemase activity.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting nucleic acid molecules that encode proteins that have racemase activity other than proline racemase activity, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use the polynucleotides that have racemase activity other than proline racemase activity in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 79 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 79 recites "...encodes an amino acid racemase activity...". It is unclear what Applicant intends. Does Applicant mean that "... encodes an amino acid sequence that has racemase activity"? Claim 79 also recites "...molecule of SEQ ID NO:7...". Does Applicant mean the nucleic acid sequence as set forth in SEQ ID NO:7?" Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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8. Claims 79-82 are rejected under 35 U.S.C 102(b) as anticipated by the Billaut-Mulot et al (*Biol. Cell*, 1994, 82(1):39-44)(*Abstract only*).

Claims 79-82 are drawn to a purified nucleic acid molecule comprising:

- (a) a molecule that hybridizes to either strand of a denatured, double-stranded DNA comprising the nucleic acid molecule of SEQ ID NO: 7 under conditions of moderate stringency and that encodes an amino acid racemase activity,
- (b) a molecule that is derived by in vitro mutagenesis from SEQ ID NO: 7 and encodes an amino acid racemase activity, and/or (c) a molecule that is degenerate from SEQ ID NO: 7 as a result of the genetic code and that encodes an amino acid racemase activity, vector, host cell comprising the purified nucleic acid molecule and a kit comprising a polynucleotide probe that hybridizes to the molecule of claim 79.

Billaut-Mulot et al et al teach a *Trypanosoma cruzi* cDNA clone corresponding to the *Trypanosoma cruzi* 45 kDa protein (see the Abstract). Billaut-Mulot et al et al teach that the trypomastigote cDNA insert was purified and subcloned into a vector (see the Abstract). Billaut-Mulot et al et al teach that the vector was expressed in *Escherichia coli* (see the Abstract). Billaut-Mulot et al et al teach that random primed cDNA hybridized to with a single 1.4 kb mRNA found in epimastigote, trypomastigote and amastigote forms. Billaut-Mulot et al et al teach that southern blot analysis were performed (see the Abstract). Therefore, the prior art teaches DNA that can hybridize to a purified nucleic acid molecule that comprises that the nucleic acid sequence as set forth in SEQ ID NO:7. The reagents that are use in hybridization reactions are inherent in the teachings of the prior art. The nucleic acid sequence as is set forth in SEQ ID NO:7 would be inherent in the teachings of the prior art. The term

"kit" constitutes an "intended use". Intended use does not impart patentable weight to a product. See MPEP 2111.03: Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967); *In re Otto*, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963). Billaut-Mulot et al et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's nucleic acid molecule with the nucleic acid molecule of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the nucleic acid molecule of the prior art does not possess the same material structural and functional characteristics of the claimed nucleic acid molecule). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

Pertinent Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure (*Verdun et al, Infection and Immunity, November 1998, p. 5393-5398*).

Status of Claims

10. No claims are allowed.

Conclusion

11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VLF
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September 8, 2005

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